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Despite nearly a decade of research, lack of consensus remains about the precise nature, etiology, and significance of Gulf War veterans' health concerns. No widely accepted case definition for Gulf War illness exists and controversy persists about whether Gulf War veterans symptoms "should be considered primarily a part of a general phenomenon that occurs in every war or a consequence of events and exposures unique to the Gulf War" (Steele, 2001, p. 406). In an effort to further elucidate the nature of ill-health among Gulf War veterans, we conducted a latent class analysis of symptoms reported in the Tenth Anniversary Gulf War Veterans Health Study, a national population-based survey of U.S. Gulf War veterans. Specifically, we sought to identify subgroups of Gulf War veterans with distinct patterns of symptoms and to determine if such subgroups could be distinguished with respect to Gulf War exposures and probable posttraumatic stress disorder (PTSD). Additionally, we sought to examine the functional consequences of specific patterns of ill-health and probable PTSD ten years after the Persian Gulf War.

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INTRODUCTION: Despite nearly a decade of research, lack of consensus remains about the precise nature, etiology, and significance of Gulf War veterans' health concerns. No widely accepted case definition for Gulf War illness exists and controversy persists about whether Gulf War veterans symptoms "should be considered primarily a part of a general phenomenon that occurs in every war or a consequence of events and exposures unique to the Gulf War" (Steele, 2001, p. 406). In an effort to further elucidate the nature of ill health among Gulf War veterans, we conduct a latent class analysis of symptoms reported in the Tenth Anniversary Gulf War Veterans Health Study, a national population-based survey of U.S. Gulf War veterans. Specifically, we sought to identify subgroups of Gulf War veterans with distinct patterns of symptoms and to determine if such subgroups could be distinguished with respect to Gulf War exposures and probable posttraumatic stress disorder (PTSD). Additionally, we sought to examine the functional consequences of specific patterns of ill-health and probable PTSD ten years after the Persian Gulf War.

BODY: This section of the final report describes the research activities and accomplishments toward completion of the approved statement of work (SOW). The approved SOW is completed, including the main analyses of the study data as described below. A report on the study sample design was presented at a professional conference and article-length manuscripts describing main study findings are in preparation for submission to peer-reviewed journals.

A. STUDY METHODS

Study design and population

The target population for this study was the estimated 689,183 U.S. Armed Forces personnel who served in the Persian Gulf region between August 1, 1990 and July 31, 1991. The study sample of 10,301 Gulf War veterans was drawn from an Operation Desert Shield/Desert Storm database maintained by the Defense Manpower Data Center. The objective of the sample design for this study was the selection of a probability sample of veterans from the target population of sufficient size to support the primary study aims of identifying reliable patterns of health concerns among Gulf War veterans and modeling the key correlates of those health concerns. Because prior research suggested that post-war health problems were more prevalent among female Gulf War veterans and individuals who had been deployed to the Gulf from the National Guard or reserves (Fukuda et al., 1998; Iowa Persian Gulf Study Group, 1997), women and reservists/National Guard were over-sampled. To obtain a sufficient number of veterans reporting significant health concerns with a sample of practicable size, we also over-sampled veterans registering with Department of Defense's (DoD) Gulf War Comprehensive Clinical Evaluation Program (CCEP) who, following medical evaluation, had received a diagnosis based on the International Classification of Diseases, 9th Revision (ICD-9-CM, 1986). CCEP participants who received an ICD-9 disorder code of Signs, Symptoms, and Ill-defined conditions were included in this stratum. To take into account an estimated 3% misclassification rate in the Operation Desert Shield/Desert Storm database, a stratified systematic sample of 10,301 was selected to achieve the target sample of 10,000.

Data collection

The human subjects committees of Duke University Medical Center, RTI International, and the U.S. Army Medical Research and Materiel Command reviewed and approved the data

collection procedures for this study. The Tenth Anniversary Gulf War Veterans Health Study (GWHS) was designed as a national population-based mail survey of a representative sample of men and women who served in all branches of the U.S. Armed Forces during the Persian Gulf War. A second phase nonresponse follow-up sample also was implemented to assess potential bias due to nonresponse and to provide important information for nonresponse adjustment as necessary. Prior to initiation of the initial mail survey, current addresses for sample members were sought through the National Institute for Occupational Safety and Health (NIOSH). In cases where NIOSH could not provide addresses or where addresses provided by NIOSH proved incorrect, RTI's tracing unit attempted to locate the sample member using a range of sources (e.g., Equifax Credit Information Service, Inc., LexisNexisTM).

There were three waves of survey mailings in Phase 1 of the GWHS. Sample members were sent an information pamphlet describing the study two weeks in advance of the first mailing of survey questionnaires, which were sent in August 2001. Questionnaires were mailed to sample members with a cover letter that explained the purpose and voluntary nature of the study; a preaddressed postage-paid return envelope was provided. A souvenir pencil was included in the wave one mailing along with a \$5.00 check. Checks were only sent to veterans who were not on active duty since military regulations prohibit active duty military personnel from receiving compensation for participating in government-funded surveys. Two weeks after the initial questionnaire mailing, sample members were sent a postcard to remind nonrespondents to complete the questionnaire and to thank respondents for their participation. In November 2001, a second questionnaire was mailed to wave one non-respondents. Calls reminding sample members to complete the survey were made to all individuals for whom a telephone number could be identified and who had not returned the survey by one month after the second mailing. A \$20.00 gift card (for veterans not currently on active duty) was enclosed with the third and final survey mailing which took place in January 2002.

In Phase 2 of the study, 1,000 nonrespondents to the mail survey were selected to participate in a follow-up telephone interview. The nonresponse follow-up survey was an abbreviated version of the mail survey conducted between June and September 2002 as a computer-assisted telephone interview (CATI). The nonresponse follow-up sample was allocated in inverse proportion to the mail survey response rates for each stratum. Firm refusals to the mail survey were excluded from selection for the nonresponse follow-up as were sample members for whom an address or telephone number could not be located despite intensive tracing efforts. Nonresponse follow-up sample members were sent a lead letter requesting their participation, along with a \$5 gift card for veterans not currently on active duty. The gift card was increased in value to \$35 if the veteran completed the follow-up telephone interview or an equivalent mail survey.

Measures

The survey instrument used in this study assessed demographic characteristics, military history, current health and functioning, and potential environmental and war zone stressor exposures during Gulf War service. The survey was constructed from standardized measures, questionnaires used in prior population-based studies of Gulf War veterans, and assessments used in studies of other military personnel. Questions about current health symptoms were adapted from earlier studies of Gulf War veterans (Fukuda et al., 1998; Iowa Persian Gulf Study Group, 1997; Unwin et al., 1999). Veterans were asked to identify symptoms with which they had had persistent or recurring problems throughout the previous 6 months or longer. For the

latent class analysis, symptoms were categorized into one of nine body systems groups: respiratory (5 symptoms), cardiovascular (2 symptoms), gastrointestinal (6 symptoms), urogenital (2 symptoms), musculoskeletal (5 symptoms), dermatological (6 symptoms), neurological (14 symptoms), psychological (7 symptoms), and general (14 symptoms). Symptom items included in each body system groups are specified in Table 1.

Symptoms of PTSD were excluded from the psychological body system group. Instead, PTSD symptoms related to veterans' experiences during the Persian Gulf War were assessed using the PTSD Checklist-Military Version (PCL). In studies of the correspondence between PCL scores and PTSD diagnoses from structured clinical interviews, a PCL cutoff score of 50 has demonstrated a high degree of diagnostic accuracy (Blanchard, et al., 1996; Weathers et al., 1993). Another approach that has been used to identify PTSD cases with the PCL is the symptom cluster method (Andrykowski et al., 1998; Weathers et al., 1993), which follows the current Diagnostic and Statistical Manual of Mental Disorders diagnostic criteria (DSM-IV; American Psychiatric Association, 1994). Because certain PTSD symptoms (e.g., difficulty concentrating) can be associated with other medical conditions, only veterans with scores of 50 or higher on the PCL who also met criteria using the symptom cluster scoring method were considered probable PTSD cases.

Indices of two syndromes previously used to characterize ill-health among Gulf War Veterans—multisymptom illness as defined by the Centers for Disease Control (CDC) and chronic fatigue—also were constructed. Cases of CDC multisymptom illness were required to have one or more chronic symptoms from at least two of the following categories: fatigue, mood/cognition, and musculoskeletal. A chronic fatigue measure was developed following the CDC definition of chronic fatigue syndrome (Fukuda et al.,1994). This measure categorized respondents as experiencing: 1) no fatigue, 2) prolonged fatigue (extreme fatigue almost every day for one month or longer during the past 6 months), or 3) chronic fatigue-like syndrome. To be designated a case of chronic fatigue-like syndrome required reporting prolonged fatigue, unrefreshed sleep, maintaining 50% or less of usual activities during the worst period, and at least four of the following symptoms—sore throat, tender glands, difficulty sleeping, muscle pain, headache, joint pain or a neurologic symptom. The study measure of chronic fatigue did not rule out exclusionary causes of fatigue (e.g., other illnesses).

The survey included several indicators of current functioning. Physical impairment was assessed using the Short Form-36 (SF-36) Physical Functioning scale (Ware, Koskinksy, & Keller, 1994). Health-related limitations in work or other regular activities due to physical or emotional problems were assessed with the SF-36 Role Physical and Role Emotional scales, respectively (Ware et al., 1994). Employment status (i.e., whether or not the veterans was currently working for pay) and income from work during the past 12 months were used as indices of functioning in the labor market.

Environmental and war zone stressor exposures during Gulf War service were assessed only in the Phase 1 mail survey; exposure data was not collected in the abbreviated nonresponse follow-up. Measures of exposure to potential environmental toxins were adapted from prior studies of Gulf War veterans (Hotopf et al., 2000; Iowa Persian Gulf Study Group, 1997). In general, low prevalence environmental exposures (e.g., receipt of botulinim toxoid vaccine) and exposures previously shown to have poor reliability were excluded from analysis (McCauley et al., 1999; Spencer et al., 2001; Wolfe et al., 2002). Days of exposure to pesticides and to smoke from oil well fires were evaluated (0, 1-30, >30 days). Additionally, a scale was created to index exposure to other petrochemicals (i.e. diesel and other petrochemicals including paint or

solvents, exhaust from heaters or generators, burning trash or feces). The internal consistency coefficient for this scale (Cronbach's alpha) was .88. Self-reported exposure to nerve gas, although potentially unreliable (McCauley et al., 1999), was retained because of a postulated link between neurotoxin exposures and ill-health among Gulf War veterans (e.g., Research Advisory Committee on Gulf War Veterans' Illnesses, 2004). Receipt of the anthrax vaccine (did not receive, don't know if received, received) and the number of pyridostigmine bromide tablets taken (0, 1-30, >30) also were evaluated.

Several measures of war zone stressor exposure were included in the survey. To assess the perceived stressfulness of living conditions and other potential low magnitude Gulf War stressors a 9-item perceived low magnitude stressor scale was developed from a review of prior research addressing Gulf War veterans' military experiences (Sutker et al., 1995; Stretch et al., 1996; Wolfe et al., 1993; Wright et al., 1995). Items (e.g., crowded living conditions or lack of privacy, long duty hours) were evaluated on a 5-point Likert scale (1=not at all stressful/did not experience to 5=extremely stressful). The internal consistency coefficient for this scale was .89. A comparable measure of the perceived stressfulness of potential high magnitude Gulf War stressor exposures (e.g., stressfulness of possibility of biological or chemical attacks) also was constructed (7 items; alpha = .89). In addition, frequency of exposure to combat and other high magnitude duty-related war zone stressors was assessed using a measure adapted by Fontana and Rosenheck (1998) from the Military Stress Inventory for Women for prior research with Gulf War veterans. An exploratory factor analysis with promax rotation was conducted to examine the structural content of Fontana and Rosenheck's war-zone stressor exposure measure. Four factors accounted for 41.5% of the overall variance; only items with factor loadings of .3 or higher were retained. The factors were labeled (1) traditional combat (e.g., under enemy fire), (2) viewing casualties (e.g., viewed a continual stream of casualties), (3) severe combat (e.g., lost communications or became cut-off from unit; knew someone who was killed, injured or missing in action), (4) duties involving death or dying (e.g., sat with someone dying from military-related causes; involved in post-mortem preparation and/or evacuation of bodies). Suffering injuries requiring medical attention was not associated with any of the factors but was retained as a separate variable because of prior research suggesting a relationship with postwar health problems (Nisenbaum et al., 2000). The experience of sexual harassment or sexual assault by other military personnel in the Gulf also was included as a potential stressor because of prior research suggesting a relationship with postwar morbidity (Wolfe et al., 1998).

Statistical analyses

Latent profile analysis was used to identify potentially meaningful subgroups of veterans on the basis of symptom reports. Latent profile analysis is an exploratory technique with some analogies to exploratory factor analysis. However, instead of grouping items into factors, cases or respondents are grouped into latent classes that explain the degree of relationship between a set of responses so that the relationship of items within class is minimized. A random subset of half the sample (balance on sampling stratum and phase) was used to examine the optimum number of classes. The number of classes that were extracted ranged from one to an undetermined maximum. Estimation (using Mplus 3.11, Muthén & Muthén, 2004) failed when extracting six or more classes, imposing a practical limit of one to five classes for comparison and implying that six or more classes were inaccurate representations of the data. The reproducibility of results was tested on the second half of the sample. Following the

identification of matching structures in the two random subsets, the sample was combined to generate the final class assignments for respondents based on model membership probabilities.

After the symptom classes had been identified, descriptive analyses were conducted to examine the relationship between symptom class and demographic characteristics, environmental and war zone stressor exposures, and current functioning. These analyses included cross-classification and the use of multinomial logistic regression that controlled for age, gender, and education. In addition, concurrent validity of the resulting symptom classes was examined through cross-tabulations with the CDC multisymptom illness and the measure of chronic fatigue.

Descriptive analyses were followed by multivariate regression models. The full model was estimated as a path model with manifest variables only (i.e., no latent factors). Factor scores for the four duty-related war zone stressor exposure factors (as suggested by the EFA described above) were obtained by confirmatory factor analysis on the full sample, saved to the full dataset and subsequently entered as manifest variables. To evaluate the extent to which the four symptom classes appeared to be conceptually distinct, dummy codes were created to test for differential effects of exposures on symptom class membership as well as to examine the potential impact on functioning that each symptom group might have.

Missing data were handled with one of two techniques, depending on which item had the missing values. All outcomes, or variables that were predicted by other measures, were simply analyzed in the model using full information maximum likelihood, an appropriate method when data are missing at random (MAR; Little & Rubin, 2002). Items that acted solely as predictors, such as the demographics, do not have distributional assumptions placed on them by the model and so they are not amenable to the FIML-based estimation in Mplus. In order to retain 810 cases that had missing values on these predictor-only items, multiple imputation (using SAS PROC MI) was used to generate five imputed datasets with plausible values of these missing values. The full model was estimated with each of these five datasets and all estimates and standard errors were combined according to Schafer's (1997) rules to yield final parameter estimate and standard errors.

Demographic items measuring gender, age, and education were used as control items for symptom report and functioning indices. Environmental and war zone stressor exposures acted as predictors of symptom class and functioning. Additionally, war zone stressor exposures and exposure to nerve gas were entered as predictors of probable PTSD. Because the directionality of the PTSD-symptom class relationship was not clear, the PTSD item and dummies indicating symptom class were correlated without a regression estimate. Symptom class and probable PTSD also were entered as predictors of functioning.

Analysis weights were developed to enable design-consistent estimation of population parameters using the methodology developed by Singh et al. (2003). All analyses were conducted using analysis weights and taking into account the sampling design. Reported n's are based on actual numbers; all percentages are weighted to reflect population parameters. Descriptive analyses (including cross-tabulations, prevalence estimation and multinomial logistic regression) were conducted in SUDAAN, release 9.0.0 (Research Triangle Institute, 2004). Factor analysis, latent profile analysis, and path analysis were all conducted using Mplus 3.11 (Muthén & Muthén, 2004).

B. RESULTS
Study population

Of the 10,301 veterans randomly selected for the study, 5182 had responded after three mailings of the Phase 1 survey. An additional 417 individuals were identified as ineligible because they either were deceased or had not been deployed to the Persian Gulf Theater during August 1990 through July 1991. Of the remaining 4702 potential participants, 4309 were estimated to be eligible for a response rate of 54.3% (using the American Association of Public Opinion Research (AAPOR) RR3 definition). Among the 1000 respondents selected for the Phase 2 nonresponse telephone follow-up, 24 were found to be ineligible and 527 participated for a response rate of 55.1%. Therefore, in total, 5,709 eligible sample members responded to either the mail survey or the telephone follow-up. The overall weighted response rate (or the effective response rate) among eligible sample members for the combined mail survey and telephone follow-up was 70.5 percent with a 95 percent confidence interval of +/- 3.3 percent. The weighted response rate can be thought of as a population parameter. That is, it is the response rate that would be achieved if everyone on the sampling frame had been selected for the survey.

Response rates were higher among females, members of the reserves/National Guard, and those who had being evaluated by the CCEP for both the Phase 1 and Phase 2 samples. Characteristics of the study populations are presented in Table 2.

Symptom subgroups

Information about the presence of 60 symptoms was organized into nine body systems as specified in the study Methods. The mean symptom values were calculated for each body system. Latent class analysis was used to examine whether subgroups of veterans could be differentiated based on their profile of symptom means across the different body systems. To examine the reproducibility of identified grouping structures, the study sample was split into two equal subsamples and initial analyses were conducted independently on each subsample. The two subsamples were constructed by randomly assigning respondents and were balanced on both the initial sampling stratum (gender, active or reserve/Guard status, and CCEP) and the sample phase (i.e. original mail survey or nonresponse follow-up respondent).

Based on the model information criteria and the probabilities of class membership for each solution, a four class solution was suggested as the best balance of fit and accuracy of classification. Classification accuracy proportions were greater then 0.90 for all four classes. A four class solution, with analogous symptom profiles was replicated in the second subsample. Final class assignments were made based on the combined sample. A total of 1953 veterans were assigned to Symptom Class 1, 1648 to Class 2, 1504 to Class 3, and 603 to Class 4. The corresponding percentages (weighted to reflect the total population) were as follows: 44.7% in Class 1; 22.8% in Class 2; 20.5% in Class 3; and 6.0% in Class 4. Comparable results supporting a four group structure also were obtained in both subsamples using cluster analysis using the k-means approach (data not shown).

Symptom means for each of the four classes are presented in Figure 1. Class 1 was comprised of veterans reporting no symptoms, or extremely low numbers of symptoms, across all systems. Class 2 reported slightly higher numbers of symptoms than Class 1 across all systems, and substantially elevated musculoskeletal symptoms. The profile for Class 3 showed higher numbers of reported symptoms across all of the body systems. Veterans in Class 4 were distinguished by reporting the highest numbers of symptoms for all nine domains. Cardiovascular, musculoskeletal, and neurological symptoms were the most frequently reported across all groups.

The distribution of symptom classes was compared to measures of CDC multisymptom illness and chronic fatigue to examine concurrent validity of the resulting class structure. While only 35.3% of those in Class 1 met criteria for CDC multisymptom illness, 86.5% of those in Class 2 and 100% of those in Classes 3 and 4 met the threshold. A similar pattern was observed for chronic fatigue. Only 5% of Class 1 qualified for prolonged fatigue and less than 1% were considered to have a chronic fatigue-like syndrome. In contrast, 10.8% of those in Class 2 had prolonged fatigue and 4.4% had a chronic fatigue-like syndrome. Rates of chronic fatigue were even higher among Class 3 (prolonged fatigue=19.3%, chronic-fatigue like syndrome =26.6%) and highest among Class 4 (prolonged fatigue=13.6%, chronic-fatigue like syndrome =65.3%).

Demographic characteristics of the four classes are presented in Table 4. In general, compared to Class 1, respondents in the other three symptom classes were older, had lower levels of education, and were more likely to have served in Iraq and/or Kuwait during the Persian Gulf War. Across each of these characteristics, the relationship tended to increase from Class 2 to Class 3 to Class 4. In addition, Classes 3 and 4 had higher percentages of female veterans and fewer Navy and Air Force personnel; Class 2 also had fewer respondents who had been in the Navy during the Persian Gulf War. Those in Classes 2 and 3 were less likely to have been officers. Other significant differences compared to Class 1 include: respondents in Class 4 were less likely to be white and more likely to have been civilians at the time of the survey; respondents in Class 2 were more likely to be married.

Relationship of exposures and current functioning to symptom class

The remainder of the study analyses focused on Phase 1 respondents because most of the exposure and functioning domains used in this study were not included in the abbreviated Phase 2 survey. Exposure and functioning characteristics of the four symptom classes are presented for Phase 1 respondents in Tables 4 and 5. Reports of environmental and war zone stressor exposures were consistently related to symptom class. Classes 2, 3 and 4 reported higher rates and/or greater levels of all exposures compared to Class 1. In addition, there was a dose response relationship such that those in Class 2 had the second highest reports of exposures, followed by Class 3, and Class 4 had both the highest rates and the highest levels of exposures. These relationships were significant even after controlling for age, gender, and education in multilog regression models. For example, more than half of the respondents in Class 4 reported being injured. Rates of injuries were almost 30% in Class 3, about 22% in Class 2 and about 15 percent in Class 1. After controlling for age, gender, and education, Class 4 veterans were more than 6.5 times as likely to report being injured compared to Class 1. Class 3 respondents were more than twice as likely (OR=2.31) to report injuries compared to Class 1 and Class 2 respondents were 63% more likely.

Symptom class was also related to probable PTSD, current functioning, income and employment. Both Classes 3 and 4 had higher rates of probable PTSD: 36.0% of those in Class 4 and 16.7% of those in Class 3, compared to 1.2% among Class 1 members. This relationship remained significant in multilog regressions models that controlled for age, gender and education. The rate of probable PTSD was not significantly higher among Class 2 veterans. Veterans in Classes 3 and 4 were also less likely to be employed, and income declined across the classes from 1 to 4. Relative to Class 1, veterans in all three more symptomatic groups had lower levels of physical functioning and reported greater role impairment due to physical and emotional problems, as measured by the SF-36.

A path model was used to simultaneously examine whether symptom classes could be distinguished with respect to Gulf War exposures and probable PTSD and the extent to which current levels of functioning were related to the symptom classes and to probable PTSD. Dummy codes were created for the symptom classes to test for differential effects of class membership in order to investigate whether the four symptom classes were conceptually distinct. Figure 1 presents significant pathways and Table 6 presents the full model results. All estimates and their associated standard errors are based on the combined values from the multiple imputation dataset analyses. Age, gender, and education were used as control variables.

No significant paths from exposures to symptom Class 2 were found, indicating that Class 1 and Class 2 were similar with respect to reported exposures. However, specific differences were noted for both Class 3 and Class 4. Perceived low magnitude stressors and petrochemical exposure were significantly related to Class 3 relative to Class 1. Perceived low magnitude stressors, sexual harassment or assault, nerve gas exposure and being injured were all significantly associated with membership in Class 4. These results may suggest a potentially different profile of exposures as related to symptom class. However, they could also reflect more of a continuum of exposure severity across one or multiple dimensions. It should be noted that additional paths were specified between war zone stressor exposures and probable PTSD to model the known association between stressor exposure and PTSD. In addition, a path between nerve gas exposure and probable PTSD was specified to address the possibility that military personnel may have considered exposure to nerve gas as potentially life threatening. Severe combat, perceived stressors (both low and high magnitude) and nerve gas exposure all were positively related to probable PTSD.

Correlational paths were specified between probable PTSD and symptom class because the specific directional relationships between these constructs could not be determined using the study's cross-sectional data. Significant correlations were found between Classes 2 through 4 and probable PTSD: Class 2 was negatively correlated with probable PTSD (r=-0.32, s.e. 0.06, z=5.47) while Classes 3 and 4 were both positively correlated with probable PTSD (Class 3 r=0.27, s.e.=0.06, z=4.74; Class 4 r=0.18, s.e.=0.08, z=2.35).

In terms of current levels of functioning, probable PTSD was negatively associated with income, current employment, and was related to poorer role functioning (greater impairment) as a result of emotional problems. After controlling for probable PTSD, symptom class was not related to either employment or income for any of the classes. However, Classes 3 and 4 were both related to poorer physical functioning and to more role impairment because of physical problems and because of emotional problems.

Paths between each of the exposures and the current functioning variables were retained to control for any direct effects they might have on functioning when we evaluated the impact of symptom class and probable PTSD on functioning. Three paths were significant: not reporting having received the anthrax vaccine was related to being employed, and reports of sexual harassment or assault were negatively related to income and positively related to physical functioning.

Invariance models were used to test for path differences between males and females in the model. The following sets of parameters were constrained to identify gender differences: (1) paths from exposures to symptom classes; (2) the correlations between probable PTSD and symptom class and (3) the paths between symptom class and probable PTSD to current functioning measures (i.e. income, employment, and SF-36 scales). There were no significant

differences in the model testing invariant paths from exposures to the symptoms classes. There were, however, significant differences when invariant correlations between symptom classes and probable PTSD were tested (p<.05). Class 3 was positively correlated with probable PTSD for males (r=0.31, s.e.=0.58) but not females (r=0.07, s.e.=0.07); conversely, Class 4 was positively associated with probable PTSD for females (r=0.46, s.e.=0.07) but not males (r=0.01 s.e.=0.84). Class 2 was negatively correlated with probable PTSD for both genders.

Tests of the invariant effects of symptom class and probable PTSD on current functioning were also significant. Employment was negatively associated with probable PTSD for males but not females. In addition, employment was negatively related to Class 4 in females, but symptom class was not associated with employment among males. Both symptom Class 4 and probable PTSD had significant negative associations with income among females, but only probable PTSD was related to income among males. The findings regarding the effects of symptom class and probable PTSD on physical and role functioning were similar: Symptom Classes 3 and 4 and probable PTSD were related to poorer functioning for both males and females.

KEY RESEARCH ACCOMPLISHMENTS: As shown in the timeline below, all key research activities in the approved SOW have been completed.

Timeline.

Activity	Months
Obtain study sample file from the Defense Manpower Data Center (DMDC; request for	30
sample submitted on 12 March 2001)	completed
Apply for and obtain clearance for revision to study incentive procedures and protocol	30-31
from the USAMRMC Human Subjects Committee and Contract Specialist.	completed
Apply for and obtain clearances for revisions to study incentive procedures and protocol	30-31
from the DUMC and RTI IRBs	completed
Submit request for current addresses of study sample to National Institute of Occupational	30-31
Safety and Health (NIOSH); obtain address file from NIOSH.	completed
Edit address file and send to National Computer Systems to format for mailing of survey	32
and related materials.	completed
Conduct and complete survey data collection activities	33-38
	completed
Plan and develop procedures for data editing and data analyses	33-38
	completed
Edit survey data and develop analysis weights	39-48
	completed
Construct analytic variables and conduct preliminary analyses.	48-60
	completed
Conduct main analyses of survey data	56-66
	completed
Present study findings at scientific meetings and prepare article-length manuscripts.	66-72
	completed

REPORTABLE OUTCOMES: Findings from the study were presented at the Joint Statistical Meeting, San Francisco, August 3-7, 2003. Paper titled "Efficient estimation for surveys with nonresponse follow-up using dual-frame calibration" that was published in the meeting proceedings (pages 3919-3930) appears in the Appendix.

CONCLUSIONS: Summary of key findings and conclusions from the Tenth Anniversary Gulf War Veterans Health Study

Extent and nature of ill-health among Gulf War veterans a decade after the Persian Gulf War

- Results of a latent class analysis identified subgroups (i.e., classes) of Gulf War veterans who evidenced varying degrees of ill-health as indicated by self reports of persistent or recurring symptoms. Approximately a decade after the Persian Gulf War an estimated 44.7% of Gulf War veterans reported low levels of symptoms across nine body systems. Relative to this comparatively asymptomatic subgroup, 28.8% of Gulf War veterans reported a substantial number of musculoskeletal symptoms but only a slightly greater number of symptoms in other body systems. An estimated 26.5% of Gulf War veterans comprised two subgroups reporting elevated symptoms across body systems, with the 6% of veterans in the fourth and smallest subgroup reporting the highest number of symptoms. Across all four veteran subgroups, the most frequently reported symptoms were those in the musculoskeletal, neurological, and cardiovascular body system groups.
- The latent class analysis also suggested that among Gulf War veterans reporting considerable symptoms, the difference in the nature of their symptoms appears to be primarily one of degree. The two subgroups of veterans reporting the greatest number of symptoms (Classes 3 and 4) were not differentiated by a distinct pattern of symptoms, but rather by the severity (i.e., number) of symptoms reported across body systems.

Association of environmental and war zone stressor exposures with ill-health

- Gulf War environmental exposures evaluated in the present study were: self-reported receipt of the anthrax vaccine, use of pyridostigmine bromide tablets, exposure to nerve gas, frequency of exposure to pesticides, frequency of exposure to smoke from oil well fires, and frequency of exposure to other petrochemicals. In bivariate analyses, using the least symptomatic subgroup (Class 1) as a reference, all environmental exposures were associated with symptom class, with veterans reporting a greater number of symptoms more likely to report each of the evaluated exposures. In a path model that controlled for potential confounding effects of multiple exposures, only frequency of exposure to petrochemicals (excluding smoke from burning oil wells) and exposure to nerve gas were associated with symptom group. Exposure to petro-chemicals was associated with Class 3 and exposure to nerve gas was associated with Class 4.
- Gulf War stressor exposures evaluated in the present study were: the perceived stressfulness of low magnitude war zone stressors, the perceived stressfulness of high magnitude war zone stressors, four factor-analytically derived measures of frequency of exposure to combat and other duty-related high magnitude stressors, being injured, and experiencing sexual harassment or assault. In bivariate analyses, veterans who were more symptomatic (those in Classes 2, 3, and 4) evaluated exposure to potential war zone stressors (low and high magnitude) as having been more stressful than did veterans reporting the fewest symptoms. Further, as was the case of environmental exposures, the remaining war zone stressor exposures evidenced a dose response relationship with symptom group such that veterans in Class 2 had the second highest reports of exposure,

followed by Class 3, and Class 4 had the highest rates and highest levels of exposures. However, in the path model only the perceived stressfulness of low magnitude war zone stressor exposures (related to Classes 3 and 4), being injured (related to Class 4), and experiencing sexual harassment or assault (related to Class 4) were associated with symptom group.

Association of probable PTSD with ill-health

In this study war-related PTSD symptoms were assessed using the military version of the PTSD checklist (PCL). Veterans who endorsed the requisite number and type of DSM-IV symptoms of PTSD and who had a PCL score of 50 or higher were designated probable PTSD cases. Using this measure, the overall prevalence of probable PTSD among Gulf War veterans approximately 10 years after the Persian Gulf War was estimated to be 7.0%. Probable PTSD prevalence rates among veterans in each of the four symptom subgroups were: 1.2% in Class 1, 2.7% in Class 2, 16.7% in Class 3, and 36.0% in Class 4. In both bivariate analyses and the path model, veterans in Classes 3 and 4 were more likely to be identified as probable PTSD cases than were veterans in Class 1.

Association of symptom group and probable PTSD with functioning indices

- Veterans' physical and role functioning one decade after the Persian Gulf War was assessed using scales from the SF-36 that measure physical impairment (SF-36 Physical Functioning), role impairment due to physical problems (SF-36 Role Physical), and role impairment due to emotional problems (SF-36 Role Emotional). Functioning in the labor market was evaluated with a measure of current employment and past year income from work. In bivariate comparisons with veterans in Class1, veterans in the more symptomatic Classes 2, 3, and 4 reported significantly poorer functioning on all three of the SF-36 scales. However in the path model symptom group was associated with decrements in physical and role functioning only for symptom Classes 3 and 4. Mean SF-36 physical and role functioning scale scores for veterans in Class 3 were approximately one standard deviation below published norms for men and women in the U.S. general populations ages 35 to 44. For veterans in Class 4, SF-36 scale means were approximately two standard deviations below published general population norms for this age group. Additionally, in bivariate analyses veterans in Classes 3 and 4 were less likely to be employed and reported lower incomes than veterans in Class 1. However, these associations were not significant in the path model.
- Prior research has reported functional impairments among veterans with PTSD. In the
 path model probable PTSD was associated with impaired role functioning because of
 emotional problems. PTSD also appeared to adversely impact functioning in the labor
 market with a diagnosis of probable PTSD evidencing negative associations with current
 employment and past year income.

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APPENDIX A: List of personnel receiving salary support from this project.

Duke University Medical Center

- 1. John A. Fairbank
- 2. Marvin Swartz
- 3. Susan Phillips
- 4. Gordon Keeler

Research Triangle Institute

- 1. Robert M. Bray
- 2. Lori Ebert
- 3. Juesta M. Caddell
- 4. Elizabeth Federman
- 5. Tzy-Mey Kuo
- 6. Jason Williams
- 7. Vincent Iannacchione
- 8. Shelton Jones
- 9. Jennifer Schoden

NCS

1. Sharon Harding

Appendix B. Tables and Figures

- **Table 1**. Symptoms items included in nine body system groups
- **Table 2**. Characteristics of Participants in the Tenth Anniversary Gulf War Veterans Health Study, Phase 1 mail survey and Phase 2 nonresponse telephone follow-up
- **Table 3.** Relationship of demographic characteristics and military history with Tenth Anniversary Gulf War Veterans Heath Study symptom subgroups
- **Table 4.** Relationship of environmental and war zone stressor exposures with Tenth Anniversary Gulf War Veterans Health Study symptom subgroups (Phase 1)
- **Table 5**. Relationship of Tenth Anniversary Gulf War Veterans Health Study symptom groups with probable PTSD, current employment, 12-month income, and current physical and role functioning (Phase 1)
- **Table 6.** Results from path model examining relationship between exposures, Tenth Anniversary Gulf War Veterans Health Study symptom groups, probable PTSD and current functioning (Phase 1)
- **Figure 1**. Symptom profiles for symptom subgroups identified via latent class analysis from Phase 1 and 2 respondents to the Gulf War Veterans Health Study
- **Figure 2**. Path model for significant associations between exposures, Tenth Anniversary Gulf War Veterans Health Study symptom groups, probable PTSD, and current functioning, controlling for age, gender and education (Phase 1)

Table 1. Symptoms items included in nine body system groups

Body system group	Symptom item
Respiratory	Shortness of breath
F	Cough
	Sore throat or irritation
	Wheezing
	Sinus problems/rhinitis
Cardiovascular	Pains in heart or chest
Cardiovascular	Heart palpitations, pounding, or racing
Gastrointestinal	Constipation
Gastromiestinai	
	Reflux, heartburn, gas or indigestion (other than during pregnancy)
	Abdominal pain (other than when menstruating)
	Frequent diarrhea (more than 3 watery stools per day)
	Nausea or an upset stomach (other than during pregnancy
	Vomiting (other than during pregnancy)
Urogenital	Frequent or painful urination
	Unusual physical discomfort in genitals during or after sexual intercourse
Musculoskeletal	Pain or aches in more than one joint
	Joint stiffness
	Back pain
	Muscle tension, aches, soreness, or stiffness
Dermatological	Skin redness or skin rash
	Dryness or scaling of skin
	Blisters, open sores, skin ulcers
	Eruptions of hives or welts on skin
	Persistent sensations of itching on skin
	Wounds that are slow to heal
Neurological	Headaches
J	Faintness, lightheadedness, dizziness or trouble maintaining balance
	Numbness or tingling in parts of your body
	Tremors or shaking
	Feeling weak in parts of your body
	Seizures/convulsions
	Loss of hearing or ringing in ears
	Double vision (when you see 2 images, not correctable by glasses)
	Problems with forgetfulness (like forgetting where you put things or forgetting
	appointments)
	Trouble finding words
	Making slips of the tongue when speaking
	Difficulty comprehending or understanding what others are saying to you
	Problems with feeling confused or disoriented in place or time (feeling confused
	about where you are, who is around, or not knowing what day it is)
Davehalasias ¹	Difficulty understanding what you read, even when you are paying attention
Psychological	Feeling depressed or blue
	Worrying or stewing about things
	Feeling no interest in things
	Difficulty falling or staying asleep
	Feeling worthless
	Feeling anxious or nervous
	Feeling moody or irritable

Table 1. (continued)

Body system group	Symptom item
General	Hot or cold spells, fever, sweats at night, or shaking chills
	Poor appetite
	Unintended weight gain of 10 lbs or more
	Unintended weight loss of 10 lbs or more
	Problems with feeling tired
	Feeling unrefreshed after sleep
	Feeling of bodily discomfort after exertion
	Any tendency to bruise or bleed easily
	Swelling of both feet or both ankles
	Mouth sores
	Unexpected hair loss
	Trouble swallowing
	Tender, painful or swollen lymph glands under your arms or in your groin
	Inflammation/redness of eyes (pink eyes)

Table 2. Characteristics of participants in the Tenth Anniversary Gulf War Veterans Health Study, Phase1 mail survey and Phase 2 nonresponse telephone follow-up

	Total	Phase 1	Phase 2
Demographic characteristics	<u>n</u> (weighted %)	<u>n</u> (weighted %)	n (weighted %)
Gender			
Male	3734 (93.2)	3381 (93.1)	353 (94.4)
Female	1975 (6.8)	1801 (6.9)	174 (5.6)
Current age	39.6 ± 0.16	39.8 ± 0.16	37.5 ± 0.50
Education			
<high school<="" td=""><td>22 (0.4)</td><td>15 (0.4)</td><td>7 (0.5)</td></high>	22 (0.4)	15 (0.4)	7 (0.5)
High school degree	893 (21.4)	786 (20.7)	107 (28.5)
Trade/some college/professional	3335 (57.9)	3020 (57.7)	315 (60.2)
College degree or higher	1432 (20.3)	1337 (21.3)	95 (10.8)
Race [†]		3	
White	3651 (68.8)	3383 (69.0)	268 (60.8)
Black	1315 (21.3)	1142 (20.5)	173 (28.7)
Other	672 (9.9)	593 (9.9)	79 (10.5)
Current marital status +		3	
Married	3895 (71.8)	3535 (72.0)	360 (68.8)
Unmarried	1781 (28.2)	1616 (28.0)	165 (30.2)
Current service status ⁺		3	
Active duty	1018 (16.5)	921 (16.5)	97 (16.7)
Reserve/Guard	981 (11.4)	908 (11.6)	73 (8.6)
Civilian	3651 (72.1)	3296 (71.9)	355 (74.7)
Prior conflict [†]			
No	4077 (79.3)	4077 (79.3)	
Yes	975 (20.7)	975 (20.7)	Not Available
Gulf War military component			
Active	3566 (83.4)	3214 (83.1)	352 (86.4)
Reserve/Guard	2143 (16.6)	1968 (16.9)	175 (13.6)
Gulf War branch of Service			
Army	4025 (50.1)	3675 (50.1)	350 (49.4)
Navy/Coast Guard	643 (23.2)	572 (23.1)	71 (23.6)
Marine Corps	461 (11.8)	404 (11.6)	57 (13.4)
Air Force	580 (15.0)	531 (15.2)	49 (13.6)
Gulf War rank			
Enlisted	4867 (88.9)	4390 (88.3)	477 (94.9)
Officer/Warrant officer	842 (11.1)	792 (11.7)	50 (5.1)
In Iraq and/or Kuwait			
No	2505 (45.7)	2310 (46.9)	195 (33.6)
Yes	3204 (54.3)	2872 (53.1)	332 (66.4)

⁺Missing data: 71 missing race, 33 missing current marital status, 59 missing current service status, 132 missing prior conflict information.

Table 3. Relationship of demographic characteristics and military history with Tenth Anniversary Gulf War Veterans Health Study symptom subgroups

	ba	Symptom subgroups sed on latent class anal	Symptom subgroups based on latent class analysis	sis		Associ	ation with sy	Association with symptom subgroups§	§sdno	
	Class 1 $(\underline{n}=1953)$	Class 2 $(\underline{n}=1648)$	Class 3 $(\underline{n}=1504)$	Class 4 (\underline{n} =603)	Class 2 v OR	Class 2 vs. Class1 JR 95% CI	Class 3 v OR	Class 3 vs. Class 1 OR 95% CI	Class 4 vs. OR	s. Class 1 95% CI
Gender Male Female	93.9 6.1	93.9 6.1	91.7	89.3	1.00	0.87, 1.33	1.00	1.31, 1.98	1.00	1.54, 3.03
Age	39.1 ±0.22	40.3±0.31	39.5±0.35	40.8±0.64	1.03***	1.01, 1.04	1.02**	1.00, 1.03	1.04***	1.02, 1.06
Education <high school<="" td=""><td>0.5</td><td>0.2</td><td>0.4</td><td>0.3</td><td>0.46</td><td>0.07, 2.94</td><td>2.51</td><td>0.54.11.77</td><td>2.30</td><td>0.01, 422.5</td></high>	0.5	0.2	0.4	0.3	0.46	0.07, 2.94	2.51	0.54.11.77	2.30	0.01, 422.5
High school degree	20.5	71	22.1	21.8	1.80**	1.26, 2.58	3.18***	2.06, 4.93	4.37***	2.23, 8.56
Trade/some college/prof.	51.5	59.0	67.1	69.4	1.82***	1.38, 2.39	3.68***	2.60, 5.21	5.02***	2.94, 8.56
Race	6.17	0.01	1.01		700.1		7.00		00:1	
			64.6	52.8	1.00		1.00		1.00	
Black	18.2	22.2	24.3	29.7	1.16	0.85, 1.57	1.28	0.89, 1.84	1.80*	1.06, 3.06
Current Marital Status				2: 1		21:1	66:1	2000	1000	,
Married	70.4	78.4	32.0	33.0	1.00	98 0 05 0	1.00	0.87 1.47	1.00	0.68 1.75
Current service status				2	20:0	20:0	20:1	20.5		21:1
Active duty	17.5	19.8	13.0	0.9	1.18	0.86, 1.61	0.75	0.56, 1.02	0.32**	0.14, 0.70
Reserve/Guard	14.0		11.0		0.58	0.41, 0.82	0.75	0.50, 1.13	0.44**	0.24, 0.82
Civilian	68.5	72.0	76.0	86.4	1.00		1.00		1.00	
Prior conflict*	2.00	702	10 0	73.0	-		1 00		5	
Yes					0.97	0.71, 1.32	1.08	0.74, 1.57	1.40	0.88, 2.24
Gulf War military										
component Active					1.00		1.00		1.00	•
Reserve/Guard	10.4	10.1	10.1	6.22	0.88	0.72, 1.09	0.95	0.77, 1.17	1.33	0.90, 1.95
Diamon of Scivice	43.1	512	58.0	9 99	9		1 30		1 00	
Navy/Coast Guard		21.0			0.66**	0.48, 0.90	0.49**	0.32, 0.75	0.52*	0.31, 0.89
Marine Corps		12.3		9.1	06.0	0.65, 1.25	69.0	0.47, 1.03	0.56	0.27, 1.15
Air Force	17.6		12.0		0.73	0.52, 1.02	0.49***	0.33, 0.73	0.13***	0.05, 0.33
Gulf War rank					•		,			
Enlisted	85.9	90.6	8.06		1.00	0000000	1.00	120 100	1.00	0.15 0.10
Officer/ Warrant officer		4.4	4.7	2.0	0.54*	0.3 / 0.80	0.36**	0.71, 0.01	0.38	0.15, 2.19
In Iraq and/or Kuwait		15.1	707	000	00		20		5	
Ves	49.3					1 04 1 62	1.00	1 26 2 07	3.03***	1 98 4 65
One respondent was not assigned to a symptom class due to missing symptom data	not assigned	to a symptor	n class due t	ve anissim o	motom data			, com (com: 1	20:5	2011

One respondent was not assigned to a symptom class due to missing symptom data

A vailable for Phase 1 sample only

\$ Results of Multinomial Logit Model, adjusted for age, gender, and education. Significance levels: * p<0.05, ** p≤0.01, *** p≤0.001

Table 4. Relationship of environmental and war zone stressor exposures with Tenth Anniversary Gulf War Veterans Health Study symptom subgroups (Phase 1)

	,,	Symptom subgroups assed on latent class anal	Symptom subgroups based on latent class analysis			Assoc	iation with	Association with symptom subgroups§	groups§	
	Class 1 (n=1736)	Class 2 (n=1592)	Class 3 (n=1334)	Class 4 (n=470)	Class 2 vs. OR	Clas 95%	Class 3 vs. Class 1 OR 95% CI	s. Class 1 95% CI	Class 4 vs. OR	s. Class 1 95% CI
Anthrax vaccine	7.30	7 00		<i>(3</i>	1 00		1 00		100	
Ves	45.6	48.6	59.0	2.C 72.C	1.00	0 93 1 60	2 82***	1 89 4 22	1.00 6.82**	2 64 17 58
Don't know	28.7			22.8	1.26	0.91, 1.76	2.31***	1.49, 3.59	3.50*	1.30, 9.45
Pyridostigmine										
bromide None	50.0	40.6	30.9	22.3	1.00		1.00		1.00	
1-30 tablets	39.0	42.8	44.8	38.6	1.33*	1.06, 1.68	1.78***	1.31, 2.44	2.13**	1.22, 3.70
>31 tablets	11.0	16.6		39.1	1.83**	1.27, 2.63	3.44***	2.31, 5.12	7.88***	4.45,13.95
Smoke from oil wells								:		
None	44.0	32.1	26.1	17.7	1.00		1.00		1.00	
1-30 days	39.0		48.1	43.3	1.67***	1.28, 2.18	2.11***	1.51, 2.94	2.86***	1.55, 5.28
≥31 days	17.0		25.8	39.0	1.72***	1.29, 2.28	2.61***	1.75, 3.88	5.90***	3.12,11.16
Pesticides										
None	64.2	56.0	40.9	25.4	1.00		1.00		1.00	
1-30 days	19.0	20.6	24.6	30.6	1.27*	1.01, 1.60	2.07***	1.52, 2.83	4.28***	2.26, 8.09
>31 days	16.8	23.4		44.0	1.60**	1.18, 2.16	3.31***	2.41, 4.54	6.75***	3.87,11.76
Petrochemicals	1.90±0.03	2.11 ± 0.03	2.35±0.03	2.49±0.06 1.66***	1.66***	1.37, 2.00	3.06***	2.45, 3.83	4.64***	3.04, 7.07
Nerve gas	0 50	8 00	7 6	069	1 00		1 00		1.00	
Yes	5.0	9.2	12.4	38.0	1.99***	1.35, 2.95	2.69***	1.72, 4.18	12.01***	6.91,20.89
Traditional combat	-0.15±0.02	0.02±0.03	0.21±0.04	0.44±0.07	1.38***	1.16, 1.64	2.18***	1.81, 2.62	3.36***	2.55, 4.42
Viewing casualties	-0.16±0.02	-0.03± 0.03	0.23±0.05	0.56±0.09	1.35***	1.16, 1.58	2.04***	1.70, 2.44	3.23***	2.52, 4.13
Duties involving										
death/dying	-0.0€±0.01	-0.005±0.01	0.08±0.02	0.21±0.04	2.74***	1.63, 4.59	5.75***	3.49, 9.46	10.74***	5.99,19.27
Severe combat	-0.20±0.02	-0.02±0.03	0.28±0.04	0.62±0.08	1.51***	1.29, 1.77	2.60***	2.16, 3.12	4.63***	3.42, 6.27
Perceived low										
magnitude Stressors	2.10±0.03	2.32±0.04	2.72±0.05	3.19±0.11	1.37***	1.21, 1.56	2.11***	1.80, 2.47	3.32***	2.67, 4.13
Perceived high	2000	700	70 0 100 0	0100	***		***	1000	4	
magnitude stressors	2.20±0.02	7.44±0.04	7.03±0.00	3.22±0.10	1.30***	1.1/, 1.45	1.80***	1.37, 2.03	7.30	2.10, 3.11
namiur Pamiur	0 70		702	140	1 00		00		1 00	
Yes	15.2	22.5		54.0	1.63**	1.21, 2.21	2.31***	1.71, 3.12	6.54***	4.25,10.05
Sexual harassment/										
assault	08 1	0 90	04.6	87.0	1 00		1 00	,	100	
Yes	1.9	3.1	5.4	12.1	1.93*	1.11, 3.36	3.1	1.87, 5.18	8.23***	4.21,16.08
§ Results of Multinomial Logit Model, adjusted for age, gender, and education. Significant Levels:	omial Logit N	Model, adjuste	d for age, genc	ler, and educa	tion. Signif	icant Levels:	* p<0.05, **	5, ** p≤0.01,	, *** p≤0.001	

Table 5. Relationship of Tenth Anniversary Gulf War Veterans Health Study symptom groups with probable PTSD, current employment, 12-month income, and current physical and role functioning (Phase 1)

Class 1 Class 2 (n=1736) (n=1592) No 98.8 97.3 Yes 1.2 2.7 ntly employed 9.3 10.6 Yes 90.7 89.5 ±1016.5 ±1102.3 cal 91.18 80.45	lass analysis			· · · · · · · · · · · · · · · · · · ·	resociation with symptom subgroups&	sed _n	
Class 1 Class 2 (n=1736) (n=1592) No 98.8 97.3 Yes 1.2 2.7 ntly employed No 9.3 10.6 Yes 90.7 89.5 45139.68 41765.58 ±1016.5 ±1102.3 cal 91.18 80.45							
No 98.8 97.3 Yes 1.2 2.7 ntly employed No 9.3 10.6 Yes 90.7 89.5 45139.68 41765.58 ±1016.5 ±1102.3	Class 3 Class 4		Class 2 vs. Class1	Class 3	Class 3 vs. Class 1	Class 4	Class 4 vs. Class 1
No 98.8 97.3 Yes 1.2 2.7 Itly employed No 9.3 10.6 Yes 90.7 89.5 45139.68 41765.58 ±1016.5 ±1102.3	$(n=1334) \mid (n=470)$	(70) OR	95% CI	OR	95% CI	OR	95% CI
No 98.8 97.3 Yes 1.2 2.7 Itly employed No 9.3 10.6 Yes 90.7 89.5 45139.68 41765.58 ±1016.5 ±1102.3 cal 91.18 80.45							
ntly employed No 9.3 10.6 Yes 90.7 89.5 45139.68 41765.58 ±1016.5 ±1102.3 cal 91.18 80.45	83.3	64.0 1.00		1.00		1.00	
ntly employed No 9.3 10.6 Yes 90.7 89.5 45139.68 41765.58 ±1016.5 ±1102.3 cal 91.18 80.45	16.7	36.0 2.16	0.93,5.02	15.43***	7.38, 32.26	41.98***	17.84.98.75
No 9.3 10.6 Yes 90.7 89.5 45139.68 41765.58 ±1016.5 ±1102.3 cal 91.18 80.45							
Yes 90.7 89.5 45139.68 41765.58 ±1016.5 ±1102.3 cal 91.18 80.45	15.2	27.1 1.00		1.00		1.00	
45139.68 41765.58 ±1016.5 ±1102.3 cal 91.18 80.45	84.8	72.9 0.94	0.63,1.43	0.63*	0.43,0.91	0.32***	0.20, 0.53
±1016.5 ±1102.3 cal 91.18 80.45	35555.89 31059.75	<u> </u>		-			
cal 91.18 80.45	±1105.4 ±2475.6	75.6	1.00, 1.00	I:00***	1.00, 1.00	1.00**	1.00, 1.00
	64.79	46.40					
Functioning ±0.56 ±1.05 ±	±1.22 ±	±2.29 0.96***	0.95,0.97	0.93***	0.92,0.94	0.91***	0.89, 0.92
91.53 79.05	51.34 2	27.96					
SF-36 Role Physical ± 0.83 ± 1.57 \pm	±2.41 ±	±3.76 0.98***	0.98,0.99	0.97***	0.96,0.97	0.95***	0.94, 0.96
90.78 83.53	54.38	29.0					
SF-36 Role Emotional ±0.89 ±1.50 ±	±2.30 ±	±3.76 0.99***	0.99,0.99	0.97***	0.97.0.98	***96.0	0.95, 0.97

\$ Results of Multinomial Logit Model, adjusted for age, gender, and education
* p<0.05
** p≤0.01
*** p≤0.001</pre>

Table 6. Results from path model examining relationship between exposures, Tenth Anniversary Gulf War Veterans
Health Study symptom groups, probable PTSD and current functioning (Phase 1)

					·
		Class 2	Class 3	Class 4	PTSD
Gulf War	Anthrax vaccine	- 0.06 (0.002)	0.08 (0.003)	0.16 (0.009)	
environmental exposures	Pyridostigmine bromide	0.02 (0.003)	0.03 (0.003)	0.13 (0.006)	
	Smoke from oil wells	0.05 (0.003)	- 0.02 (0.003)	0.10 (0.007)	
	Pesticides	- 0.05 (0.002)	0.08 (0.002)	0.13 (0.006)	-
	Petrochemicals	0.10 (0.004)	0.25 (0.005)*	- 0.00 (0.013)	
	Nerve gas	- 0.03 (0.012)	- 0.20 (0.012)	0.55 (0.020)*	0.46 (0.022)*
Gulf War war zone stressor	Traditional combat	0.02 (0.009)	- 0.00 (0.011)	- 0.12 (0.022)	- 0.34 (0.029)
exposures	Viewing casualties	- 0.08 (0.008)	- 0.06 (0.009)	0.03 (0.020)	- 0.18 (0.021)
	Duties involving death/dying	0.12 (0.023)	0.03 (0.026)	- 0.18 (0.056)	0.01 (0.046)
	Severe combat	- 0.03 (0.017)	0.23 (0.020)	0.27 (0.043)	0.65 (0.049)*
	Perceived low magnitude stressors	- 0.07 (0.003)	0.19 (0.004)*	0.31 (0.008)*	0.30 (0.008)*
	Perceived high magnitude stressors	0.04 (0.003)	- 0.00 (0.003)	- 0.06 (0.008)	0.27 (0.008)*
	Injured	0.01 (0.007)	0.03 (0.007)	0.45 (0.014)	0.24 (0.016)
	Sexual harassment/assault	- 0.01 (0.022)	- 0.02 (0.018)	0.44 (0.029)*	0.06 (0.027)
Current functioning	Employment	- 0.07 (0.004)	0.05 (0.004)	- 0.07 (0.006)	- 0.42 (0.006)*
	Income	- 0.05 (0.008)	- 0.05 (0.006)	- 0.14 (0.007)	- 0.57 (0.013)*
	SF-36 Physical Functioning	- 0.52 (0.596)	- 5.85 (0.391)*	- 8.31 (0.661)*	- 4.10 (0.875)
	SF-36 Role Physical	0.41 (1.509)	-10.08 (1.403)*	-12.64 (2.018)*	- 7.66 (2.963)
	SF-36 Role Emotional	1.69 (1.915)	- 7.33 (1.551)*	-10.48 (2.218)*	-10.95 (2.950)*
Demographic controls	Age	0.01 (0.000)*	0.00 (0.000)	0.01 (0.000)	
COHUOIS	Gender	- 0.10 (0.006)	0.21 (0.007)*	0.13 (0.014)	
	Education	- 0.07 (0.001)*	- 0.16 (0.002)*	- 0.15 (0.003)*	

^{*} p<0.05

Figure 1. Symptom profiles for symptom subgroups identified via latent class analysis from Phase 1 and 2 respondents to the Gulf War Veterans Health Study

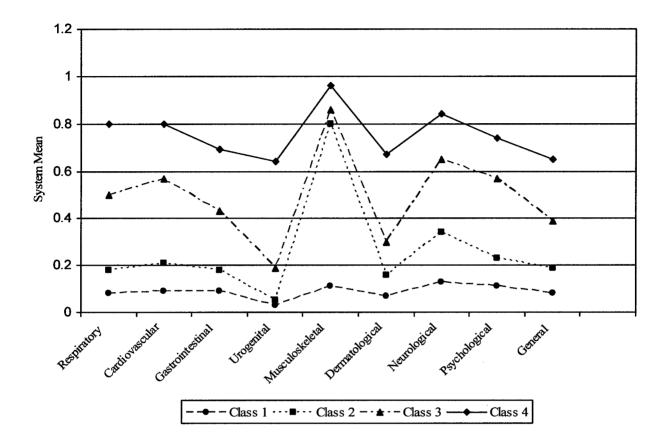


Figure 2. Path model for significant associations between exposures, Tenth Anniversary Gulf War Veterans Health Study symptom groups, probable PTSD, and current functioning, controlling for age, gender and education (Phase 1

